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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/283,431	04/01/1999	WEN-QIANG ZHOU	475.08.423	9988

7590 02/08/2006
WAYNE A KEOWN
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60 STATE STREET
BOSTON, MA 02109

EXAMINER

VIVLEMORE, TRACY ANN

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/283,431

Applicant(s)

ZHOU ET AL.

Examiner

Tracy Vivlemore

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1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 September 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Any rejection not reiterated in this Action is withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 6, 2005 has been entered.

Priority

The priority date for the claimed invention is the filing date of the instant application, April 1, 1999. No support could be found in provisional application 60/080321 for the claimed embodiment of deoxyribonucleotide POPS blocks. If applicant believes such support exists in the provisional application, it should be pointed out with particularity in the response to this action.

Double Patenting

Claims 4-11 remain provisionally rejected and new claims 12-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4-8 of copending Application No. 10/291,058.

Applicant has previously noted that a provisional obviousness-type double patenting rejection will be withdrawn when it is the only remaining rejection. However, until this should happen it is proper that the provisional obviousness-type double patenting rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 4-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Manoharan (US 6,277,967, cited on IDS).

The claimed invention is directed to hybrid oligonucleotides comprising a region of deoxynucleosides linked by alternating phosphodiester and phosphorothioates linkages flanked by regions of 2'-O-substituted ribonucleosides having linkages chosen from the group consisting of phosphodiester and phosphorothioate. The oligonucleotides are 12-50 or 17-35 nucleotides in length and the alternating phosphorothioate/phosphodiesters are present in ratios of 3:1 to 1:3. The 2'-O-substitutions are halogen, O-alkyl, aryl or allyl.

Manoharan discloses oligonucleotides having the formula shown in claim 7, comprising alternating phosphodiester and phosphorothioate linkages in a 1:1 ratio wherein the 2' sugar position can be deoxy, fluoro or O-alkyl, -alkenyl or -alkynyl. One of these oligonucleotides is a 20mer shown in column 27 as SEQ ID NO: 2. This oligonucleotide comprises ribonucleosides having 2'-MOE substitutions, a region of 2'-deoxy nucleosides and a second region of ribonucleosides having 2'-MOE substitutions.

Thus, Manoharan discloses all limitations of and anticipate claims 4-14.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manoharan.

The claimed invention is directed to inverted hybrid oligonucleotides comprising a region of 2'-O-substituted ribonucleosides having linkages chosen from the group consisting of phosphodiester and phosphorothioate flanked by regions of deoxynucleosides linked by alternating phosphodiester and phosphorothioates linkages. The oligonucleotides are 12-50 or 17-35 nucleotides in length and the alternating phosphorothioate/phosphodiesters are present in ratios of 3:1 to 1:3. The 2'-O-substitutions are halogen, O-alkyl, aryl or allyl.

Manoharan discloses oligonucleotides having the formula $W^1-W^2-W^3$, shown in claim 13, wherein W^1 and W^3 comprise alternating phosphodiester and phosphorothioate linkages wherein the 2' sugar position can be deoxy, fluoro or O-alkyl, -alkenyl or -alkynyl and W^2 is a plurality of covalently bound nucleosides linked by phosphodiester or phosphorothioate linkages. Although Manoharan is silent as to the presence of 2'-O-substitutions in the region designated as W^2 , the production of such oligonucleotides would be recognized by one of ordinary skill in the art to be mere design choice based on Manoharan's teaching of oligonucleotides having 2'-O-substitutions. One of ordinary skill in the art would have had a reasonable expectation of success in producing oligonucleotides having the formula shown in claim 13 wherein W^2 comprises 2'-O-substitutions because Manoharan teach that synthesis of oligonucleotides having such substitutions is well-known and routine in the art.

Thus, the invention of claims 15-25 would have been obvious, as a whole, at the time of invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It

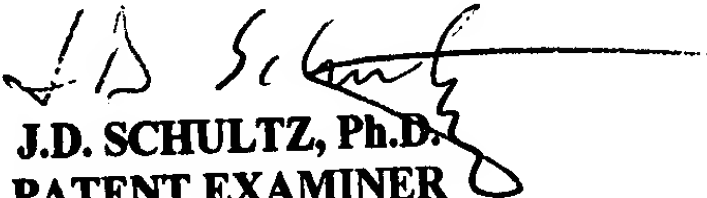
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also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
February 2, 2006


J.D. SCHULTZ, Ph.D.
PATENT EXAMINER